I. Election/Restriction

The Restriction Requirement has been deemed proper and made final, restricting the invention into Groups I and II. Accordingly, Applicants are canceling without prejudice Group II, claims 15-20, reserving the right to file continuing applications on the canceled subject matter. Applicants affirm the election of claims 1, 2 and 4-14.

II. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claims 11-14 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner suggests that claim 11 recites the phrase "...a compound ... which specifically hybridizes with at least an 8 nucleobase portion of an active site..." where the term active site is not defined in the specification and it is unclear what is meant by that term. Applicants respectfully point out that at page 83, lines 3-12 of the specification as filed, the term active site is indeed defined as being the target sites listed in Table 1. Therefore, contrary to the Examiner's suggestion, the term is defined such that one of skill would be able to understand its meaning. However, in an earnest effort the advance the

prosecution, claim 11 has been canceled. Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 102(b)

Claims 1, 2 11 and 12 have been rejected under 35 U.S.C. 102(b) and 103(a) as being anticipated by Soh et al. (1994). The Examiner suggests that this reference teaches a probe that is 20 mer and was used to screen a library comprising SEQ ID NO: 3 and although the reference does not specifically teach antisense or use of oligonucleotides to inhibit gene expression, the probe of Soh et al. was used in gene isolation and was antisense so it would inherently inhibit expression of the gene. Applicants respectfully traverse this rejection.

At the outset, Applicants have amended claim 1, and by dependency claim 2, to recite that the compounds of the instant invention are targeted to specific regions within the sequence of interferon gamma receptor 2 of SEQ ID NO: 3. Support for these amendments to the claims can be found throughout the specification as filed but in particular at pages 80-83.

Soh et al. (1994) disclose a probe that is complementary to the coding region of SEQ ID NO: 3 at positions 979-998 only. Applicants respectfully disagree with the Examiner's suggestion

that a probe complementary to the sense strand of the gene would inherently inhibit expression of the target gene, making this reference not anticipating of the instant invention where antisense compounds have the ability to inhibit gene expression. However, in an earnest effort to advance the prosecution, Applicants have canceled claim 11 and amended claim 1, and by dependency claims 2 and 12, as discussed supra, to refer to targeting regions of SEQ ID NO: 3 with antisense, regions that do not include nucleobases 979-998 of the coding region. Accordingly, withdrawal of this rejection is respectfully requested.

IV. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 4-10, 13 and 14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Soh et al. (1994), in view of Monia et al. (US Patent 6,043,090). The Examiner suggests that it would have been *prima facie* obvious to one of ordinary skill to combine the teachings of Soh et al. (1994) and Monia et al. to create antisense oligonucleotides as claimed, including the modifications cited in the claims. The Examiner suggests that one of skill would have been motivated to combine the references by Monia who teaches that modified oligonucleotides are desirable. Applicants respectfully traverse this rejection.

At the outset, claim 1 and its dependent claims (4-10, 13 and 14) have been amended as discussed *supra* to recite antisense compounds targeted to specific regions of human interferon gamma receptor 2 of SEQ ID NO. 3.

As discussed *supra*, Soh et al. fail to teach or suggest antisense compounds as claimed which are targeted to specific regions of human interferon gamma receptor 2 of SEQ ID NO: 3, specific regions other than the region encompassed by nucleobases 979-998. Therefore, these primary reference fails to teach the limitations of the claims as amended.

The secondary reference cited fails to overcome the deficiencies in teaching of the primary reference.

Monia et al. (US Patent 6,043,090) discloses antisense compounds that target the Akt-1 gene, as well as a general teaching of ways to modify antisense compounds in order to increase activity. However, nowhere does this patent teach or suggest antisense oligonucleotides 8 to 50 nucleobases in length targeted to human interferon gamma receptor 2 of SEQ ID NO: 3, or any region of such a nucleic acid molecule.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in

the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to specific regions of human interferon gamma receptor 2 of SEQ ID NO. 3, and thus cannot render the instant claimed invention obvious. Further, the cited references fail to provide an expectation of success as it is only with the specification in hand that one of skill would understand how to make and use the claimed antisense, in particular what regions of the gene to target with antisense as now claimed, and thus have an expectation of success at developing antisense to target SEQ ID NO: 3. Withdrawal of this rejection is therefore respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

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Inventors: **Bennett and Watt**
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Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

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Registration No. 32,257

Date: **February 3, 2003**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 11 and 15-20 have been canceled without prejudice.

Claim 1 has been amended as follows:

1. (Twice amended) A compound 8 to 50 nucleobases in length targeted to a 5'-untranslated region, nucleobases 741 through 760, nucleobases 769 through 805, nucleobases 818 through 837, nucleobases 845 through 936, nucleobases 955 through 978, nucleobases 1000 through 1092, nucleobases 1144 through 1163, nucleobases 1180 through 1220, nucleobases 1233 through 1285, nucleobases 1291 through 1389, nucleobases 1399 through 1445, nucleobases 1496 through 1533, nucleobases 1540 through 1559, nucleobases 1575 through 1620 of a coding region, a stop codon region, or a 3'-untranslated region of a nucleic acid molecule encoding human interferon gamma receptor 2 (SEQ ID NO: 3), wherein said compound specifically hybridizes with one of said regions and inhibits the expression of human interferon gamma receptor 2.

The extension of time fee transmitted herewith is paid at the Large Entity rate.

Respectfully submitted,

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Date: February 3, 2003

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